

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	1	Carcagno SAME miguel SAME carlos	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/07/11 10:16
L2	484	(human NEAR recombinant NEAR erythropoietin)". clm"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/07/11 10:24
L3	108	(erythropoietin SAME (CHO COS BHK Namalwa HeLa)) SAME insulin	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/07/11 10:25
L4	6	(human NEAR recombinant NEAR erythropoietin) SAME insulin	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/07/11 10:26
L5	484	human NEAR recombinant NEAR erythropoietin	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/07/11 10:26
L6	184	(tangential NEAR filtration ) and erythropoietin	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/07/11 10:26
L7	6	(Tangential WITH flow WITH filtration.clm.) and (erythropoietin or epo)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/07/11 10:27
L8	59	erythropoietin SAME frozen	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/07/11 10:27

j => d his

(FILE 'HOME' ENTERED AT 10:48:53 ON 11 JUL 2005)

FILE 'MEDLINE, CANCERLIT, AGRICOLA, CAPLUS, SCISEARCH' ENTERED AT  
10:49:25 ON 11 JUL 2005

L1	13297 S HUMAN ERYTHROPOIETIN
L2	283205 S CHO OR COS OR NAMALWA OR HELA
L3	218 S L1 (L) L2
L4	121 DUP REM L3 (97 DUPLICATES REMOVED)
L5	68 S L4 AND PY<=1998
L6	4 S L5 AND DMEM
	E CARCAGNO CARLOS MIG?/AU
L7	4 S E4
L8	4 DUP REM L7 (0 DUPLICATES REMOVED)

d his

(FILE 'HOME' ENTERED AT 10:48:53 ON 11 JUL 2005)

FILE 'MEDLINE, CANCERLIT, AGRICOLA, CAPLUS, SCISEARCH' ENTERED AT  
10:49:25 ON 11 JUL 2005

L1 13297 S HUMAN ERYTHROPOIETIN  
L2 283205 S CHO OR COS OR NAMALWA OR HELA  
L3 218 S L1 (L) L2  
L4 121 DUP REM L3 (97 DUPLICATES REMOVED)  
L5 68 S L4 AND PY<=1998  
L6 4 S L5 AND DMEM

=> d an ti so au ab pi l6 1-4

L6 ANSWER 1 OF 4 MEDLINE on STN  
AN 1998294721 MEDLINE  
TI Production of rhEPO with a serum-free medium in the packed bed bioreactor.  
SO Chinese journal of biotechnology, (1997) 13 (4) 247-52.  
Journal code: 9100855. ISSN: 1042-749X.  
AU Deng J; Yang Q; Cheng X; Li L; Zhou J  
AB Recombinant CHO (C2) cells producing human erythropoietin (rhEPO) were cultured with DMEM:F12 media containing 5% FBS for 8-10 days in a packed bed bioreactor, then rhEPO was produced with a serum-free medium (SFM-p) which was prepared in our laboratory. The SFM-p medium can support the growth of C2 cells and the production of rhEPO, and furthermore, it easily separates rhEPO from the culture supernatant. The cell culture in a packed bed bioreactor system using SFM-p was maintained in a stable condition for 20-25 days. The expression level of rhEPO was 12-28.4 mg/L. The bioreactor productivity was 71.0 mg/L.d and increased by 12-14 fold over that of the roller bottle. The glucose consumption rate was 21 g/L.d. At the end of 30 days of perfusion circulation, a final cell density of over  $3.0 \times 10^7$ /ml of culture volume was achieved. Since the cells were entrapped in the polyester disk, the culture supernatant contained only a few detachment cells. Variations in lactate and ammonia production in the reactor were observed, and results showed that the productions of lactate and ammonia by the bioreactor were 3.5 g/L and 5 mmol/L, respectively, and did not affect the expression of interest protein. This experiment demonstrates that SFM-p is suitable for the growth and rhEPO production of recombinant C2 in the packed bed bioreactor.

L6 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2004:844103 CAPLUS  
DN 142:54832  
TI Purification of recombinant human erythropoietin using immunoadsorption chromatography  
SO Repub. Korea, No pp. given  
CODEN: KRXXFC  
IN Oh, Myung Suk; Kim, Hyun Soo; Lee, Dong Uk; Ha, Byung Jip; Yoo, Ree Ahn; Kim, Suk Joon; Park, Wan Je; Lee, Sang Ok  
AB Provided is a purification method for recombinant erythropoietin (EPO) which removes impurities such as DNAs, monoclonal antibodies, endotoxins, and EPO polymers by loading EPO into monoclonal antibody column, hydroxyapatite column and an ion exchange resin column. CHO cell, CHOEp-cfc33 (KCLRF BP\_00007), transfected with EPO gene is cultured in DMEM: F12 mixed medium containing 5 % of fetus bovine serum albumin for 3 days. Ten L of culture broth is centrifuged to remove cells and supernatant is collected. Monoclonal antibody of EPO is obtained from cfc-8 and cfc-9 originated from fused cell of NO-S and splenocyte cell of EPO immunized cell. Ammonium sulfate precipitation and column chromatog. are applied to purify monoclonal antibody. Sepharose-4B resin is used to immobilize EPO monoclonal antibody. The final purified EPO is tested by RIA and LAL test to quantify the amount of coeluted EPO antibody and no EPO antibody is detected.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
KR 153808	B1	19981015	KR 1994-32994	19941206 <--

L6 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:415436 CAPLUS  
DN 129:242110  
TI Production of rHuEPO with serum-free medium in packed bed bio-reactor  
SO Shengwu Gongcheng Xuebao (1997), 13(4), 375-379  
CODEN: SGXUED; ISSN: 1000-3061  
AU Deng, Jixian; Yang, Qin; Cheng, Xun; Li, Lin; Zhou, Jiang  
AB Recombinant CHO(C2) cells producing human erythropoietin were cultured with 5% FBS DMEM, F12 medium for 8-10 days in packed bed bio-reactor, then rHuEPO was produced with self-made serum-free medium (SFM-p). SFM-p medium could support the growth of C2 cells and the production of rHuEPO. Moreover, rHuEPO was easily separated from the culture supernatant. Cell culture in the packed bed basket system using SFM-p was maintained in a stable condition for 20-25 days. The expression level of rHuEPO was 12-28.4 mg/L. The bio-reactor productivity was 71.0 mg/L.d and increased 12-14-fold over that of the roller bottle. Glucose consumption rate was 21 g/L.d. A final cell d. of over  $3.0 \times 10^7$ /mL of culture volume was achieved at the end of 30 days of continuous perfusion culture. The culture supernatant contained a few of detachment cells since the cells were entrapped in the polyester disks. Variations in lactate and ammonia production between the reactor and roller bottle were observed. It showed that lactate and ammonia production of bio-reactor were 3.5 g/L and 5 mmol/L resp., and did not affect the expression of interest protein. The experiment demonstrates that SFM-p is suitable to the growth and rHuEPO production of recombinant C2 in the packed bed bioreactor.

L6 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1998:261609 CAPLUS  
DN 129:104852  
TI Serum-free medium used for production of recombinant human erythropoietin  
SO Junshi Yixue Kexueyuan Yuankan (1997), 21(4), 244-246  
CODEN: JYKYEL; ISSN: 1000-5501  
AU Deng, Jixian; Yang, Qin; Cheng, Xun; Li, Lin; Lu, Jianshen  
AB Various additives of serum-free medium suitable to CHO cells were screened based on the consumption of medium compns. of C2 cells producing recombinant human erythropoietin (Rhuepo). Se, Ethanolamine, lipid, various vitamins, peptone, insulin, transferrin and some cytokines were added in a DMEM:F12 (1:1) medium to constitute the serum-free medium named SFM-p. It contained no bovine serum albumin but could support the growth and Rhuepo production of C2 cells. Productivity of Rhuepo with SFM-p was the same as that with 1% FBS medium in rolling bottles. The same studies were conducted in a packed bed bioreactor for C2 cells by using SFM-p. The C2 cells were cultured with 5% FBS medium for 9 days, then substituted with SFM-p. Cell culture in SFM-p could be maintained in a stable condition of Rhuepo production for 20 days in the bioreactor. The Rhuepo productivity in a bioreactor was 71.0 mg/(L.d), and the culture supernatant contained 28.4 µg/mL of Rhuepo. Glucose consumption rate was 21 g per L per day. The highest d. of cells could exceed  $3.0 \times 10^7$  cells/mL, and Rhuepo could be easily separated from the culture supernatant. Thus, SFM-p can maintain the growth and recombinant human erythropoietin production in recombinant C2 cells.

=>